

296. A method of reducing cellular production of amyloid beta (A $\beta$ ) from amyloid precursor protein (APP), comprising steps of:

- (a) identifying mammalian cells that produce A $\beta$ ; and
- (b) transforming or transfecting the cells with an anti-sense reagent capable of reducing Asp1 polypeptide production by reducing Asp1 transcription or translation in the cells, wherein reduced Asp1 polypeptide production in the cells correlates with reduced cellular processing of APP into A $\beta$ .

297. A method according to claim 296, wherein the identifying step comprises diagnosing Alzheimer's disease, where Alzheimer's disease correlates with the existence of cells that produce A $\beta$  that forms amyloid plaques in the brain.

298. A method according to claim 295 or 296, wherein the cell is a neural cell.

299. A method according to any one of claims 298, wherein the anti-sense reagent comprises an oligonucleotide comprising a single stranded nucleic acid sequence capable of binding to a Hu-Asp1 mRNA.

300. A method for the identification of an agent that decreases the activity of a Hu-Asp polypeptide selected from the group consisting of Hu-Asp1, Hu-Asp1(a), and Hu-Asp2(b), the method comprising

- (a) determining the activity of said Hu-Asp polypeptide in the presence of a test agent and in the absence of a test agent; and
- (b) comparing the activity of said Hu-Asp polypeptide determined in the presence of said test agent to the activity of said Hu-Asp polypeptide determined in the absence of said test agent;

whereby a lower level of activity in the presence of said test agent than in the absence of said test agent indicates that said test agent has decreased the activity of said Hu-Asp polypeptide. --

## REMARKS

By the foregoing, the Applicants have amended the claims to delete multiple dependencies to reduce the filing fee and not for any reasons related to patentability. Support for new claims 151-300, which mirror Applicants' published Article 19 claims, is found throughout the specification. The Applicants do not intend by these or any other amendments to abandon the subject matter of any claim as originally filed, and reserve the right to pursue such subject matter in this or related applications, including but not limited to parent and continuing applications.

This amendment is submitted to put the specification in better compliance with the requirements for patent applications containing nucleotide sequence and/or amino acid sequence disclosures pursuant to 37 CFR §1.821-1.825. The foregoing amendments to the specification insert sequence identification numbers within the specification as required by 37 C.F.R. 1.821(d).

The substitute Sequence Listing that is part of this amendment assigns sequence identification numbers to sequences that were present in the application as filed but were not assigned a sequence identification number. The substitute sequence listing also corrects the nucleotide sequences of SEQ ID NOS: 47-49. The sequence listing as originally filed contained nonsense characters within SEQ ID NOS: 47- 49. Support for the correct nucleotide sequences of SEQ ID NOS: 47-49 is found on page 39 lines 19-23 of the specification. Support for new SEQ ID NOS: 50-58 is found throughout the specification. The amendment adds no new matter because all sequences added to the sequence listing are present and find support in the application as filed.

**CONCLUSION**

These amendments put the application in better compliance with the sequence rules set out in 37 CFR § 7.821-1.825. The Applicants request entry of this amendment.

Respectfully submitted,

MARSHALL, O'TOOLE, GERSTEIN,  
MURRAY & BORUN

By



David A. Gass  
Registration No. 38,153  
Attorneys for Applicants  
6300 Sears Tower  
233 South Wacker Drive  
Chicago, Illinois 60606-6402  
(312) 474-6300

March 26, 2001